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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/724,254	11/28/2000	Riccardo Dalla-Favera	58044-A/JPW/EMW	5325

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EXAMINER	
CANELLA, KAREN A	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 06/04/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,254	DALLA-FAVERA, RICCARDO	
	Examiner	Art Unit	
	Karen A Canella	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25,33-47,69 and 70* is/are pending in the application.

4a) Of the above claim(s) *1-25 and 32-42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *43-47,69 and 70* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *9/4/2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 45-47 have been amended. Claims 69 and 70 have been added. Claims 1-25, 33-47, 69 and 70 are pending. Claims 1-25 and 32-42 remain withdrawn from consideration. Claims 43-47, 69 and 70 are under consideration.

2. Applicant's claim to an earlier effective filing date via provisional application 60/168,151 is hereby recognized in light of applicant's argument regarding figures 6a-c of the provisional application.

3. Applicant has deleted reference to the browser-executable code "without conceding to the correctness of the Examiner's objection". Applicant is referred to section 608.1 of the M.P.E.P. Deletion of Browser executable code is a PTO-policy, not subject to the judgment of the examiner.

4. The rejection of claims 43-47 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is maintained for reason of record. Claims 69 and 70 are also rejected for the same reasons of record.

The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 43-47, 69 and 70 are drawn to antibodies which are directed to the IRTA2 protein. The specification describes the IRTA proteins as belonging to the immunoglobulin superfamily receptor translocation associated genes which are differentially targeted by 1q21 abnormalities (page 4, line 32 to page 5, line 7). The specification provides a description to three isoforms of IRTA2 (a, b and c) resulting form alternate splicing (figure 18B) and set forth as SEQ ID NO: 44, 3 and 41, respectively . The specification concludes that the IRTA family may represent an intersection among the Fc, IRS and Cam families, combining features from all three. When given the broadest reasonable interpretation, the claims are dependent upon a genus of proteins which belong to the immunoglobulin receptor superfamily and are deregulated as a result of a 1q21 abnormality. The genus of proteins encompasses other alternatively spliced variants comprising sequences similar

to Fc, IRS and CAm proteins. The genus is highly varied as structural attributes which define the proteins of the genus are missing from the claims. Further there is no nexus between one translocation associated gene and another, because the art teaches that translocations are random events and cannot be predicted. Accordingly SEQ ID NO: 44, 3 and 41 fail to describe this genus, because the genus encompasses proteins having varied structural and functional attributes. One of skill in the art would conclude that applicant did not disclose a representative number of species of the protein genus and therefore was not in possession of the antibodies which bound to the proteins of the genus.

Applicant argues that the claimed genus is supported by the disclosed species and that the species disclose the necessary attributes of the genus. However, applicant does not point out what specific structural and functional attributes of the disclosed species determine the structural and functional attributes of the genus of IRTA2 proteins.

5. The rejection of claims 43 and 44 under 35 U.S.C. 102(b) as being anticipated by the abstract of Medesan et al (Revue Roumaine de Biochimie, 1979, Vol. 16, pp. 31-47) is maintained for reasons of record. New claim 69 is also rejected for the same reasons of record.

Claim 43 is drawn to an antibody directed to a purified IRTA2 protein. Claim 44 specifies that the protein is a human IRTA2 protein.

The specification teaches that IRTA2c which is a human protein can specifically bind heat aggregated human serum IgG (page 80, lines 13-14).

Medesan et al disclose heat aggregated human IgG, thus fulfilling the specific embodiments of the claims.

6. Claims 43-45 are rejected under 35 U.S.C. 102(b) as being anticipated by Zipf et al (Journal of Immunology, 1983, Vol. 131, pp. 3064-3072) as evidenced by the abstract of Callanan et al (Blood, 1998, Vol. 92, No. 10, suppl 1, page 2445) and as evidenced by Macardle et al (European Journal of Immunology, 2002, Vol. 32, pp. 3736-3744). Claim 46 is also rejected for the same reasons of record, although it was inadvertently left out of the previous Office action due to a typographical error.

Zipf et al disclose a monoclonal antibody of 41H.16. Macardle et al disclose that the 41H16 antibody is an anti-CD32 antibody binding to FcgammRIIb (page 3737, second column, first sentence under the heading of section 2.1). The abstract of Callahan et al discloses that a cell line derived from a patient having follicular lymphoma exhibiting overexpression of FcgammaRIIb2 and that this cell line had a 1q21 translocation (t(1;22)(q21;q11)). The specification states on page 71, lines 5-23, that IRTA2 mRNA expression is highest in centrocytes and post-germinal center B cells, consistent with detection of mRNA for IRTA2 in intraepithelial and intrafollicular regions of the tonsils. The specification states on page 74, lines 26-27, that IRTA2 expression is frequently deregulated in cell lines carrying 1q21 abnormalities. One of skill in the art would conclude that the FcgammaRIIb has the same characteristics as that disclosed for the IRTA2, as both proteins are immunoglobulin receptors, and both proteins are deregulated as a result of a 1q21 abnormality. Thus the anti CD32 antibody fulfills the specific embodiments of the claims .

7. Applicant argues that neither the disclosure of Medesan et al nor the disclosure of Zipf et al meet the claim limitations because IRTA2 is not described therein. This has been considered but not found persuasive. The claims are drawn to antibodies which bind to IRTA2. It is not necessary to describe IRTA2 in order to disclose an antibody which can bind to IRTA2 because antibodies are known to react with proteins based on the recognition of an epitope wherein said epitope is either a three dimensional or contiguous linear structure. The instant specification teaches that heat aggregated human serum IgG can bind to IRTA2c, therefore the binding of said IgG to IRTA2c is not disputed. Medesan et al discloses heat aggregated human serum IgG which fulfills the specific embodiments of the claims.

Applicant argues that the disclosed IRTA2 amino acid sequences differ from the sequence of Fcgamma RIIb and that the translocation which produced the Fcgamma RIIb of Zipf et al differs from the translocation disclosed in the specification. This has been considered but not found persuasive. Applicant states that the translocation disclosed by Callahan et al is a q12:q11 translocation. This is incorrect. Callahan describes the translocation as a t(1;22)(q21;q11) and is thus a 1q21 translocation. It is not necessary that the Fcgamma RIIb have the same amino acid sequence as the instant IRTA2, it is only necessary that the

monoclonal antibody 41H.16 bind to a 3-dimensional or contiguous epitope of IRTA2 . Further, because the IRTA2 genus encompasses splice variants and proteins encoded by polynucleotide unregulated as a result of a 1q21 translocation, the Fcgamma RIIb can be considered a IRTA2 protein. Applicant has not provided evidence that said monoclonal antibody does not bind to IRTA2, therefore the rejection is maintained.

8. The rejection of claims 43-47 under 35 U.S.C. 103(a) as being unpatentable over Schlom ("Monoclonal Antibodies :They're More and Less Than You Think", In: Foundations of Oncology, 1991, Broader, Ed., pp. 95-134) in view of Zipf et al (Journal of Immunology, 1983, Vol. 131, pp. 3064-3072) and the abstract of Callanan et al (Blood, 1998, Vol. 92, No. 10, suppl 1, page 2445) and Macardle et al (European Journal of Immunology, 2002, Vol. 32, pp. 3736-3744) and Latour et al (Journal of Immunology, 1996, Vol. 157, pp. 189-197) is maintained for reasons of record. New claims 69 and 70 are also rejected for the same reasons of record.

Schlom teaches anti-tumor antibodies conjugated to drugs, toxins and radionuclide for enhancement of targeting said drugs, toxins and radionuclide to tumors. (pages 107-109) Schlom teaches that in order to be useful, said conjugates must be internalized for cytotoxic activity to occur (page 107, second column, lines 5-10 under the heading "Drug and Toxin mAb Conjugates"). Schlom does not specifically teach an antibody directed to FcgammIIb2.
Latour et al teach that antibodies which bind to FcgammaRIIb2 are internalized versus antibodies which bind to FcgammaRIIb1, which are not internalized (page 192, first column, lines 11-17, under the heading "Biologic activities of 32-kDa FcgRIIB").

The combination of Zipf et al, the abstract of Callahan et al nor Macardle et al teach the anti CD32 antibody which binds to the FcgammaRIIb2 and the overexpression of FcgammaIIb2 in a cell line derived from a lymphoma patient having a 1q21 abnormality.
It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to conjugate the anti-Cd32B antibody to a drug, toxin or radionuclide as taught by Schlom.

One of ordinary skill in the art would have been motivated to do so with a reasonable expectation of success by the teachings of Zipf et al, the abstract of Callahan et al and Macardle, which render obvious the anti-Cd32B antibody for targeting FcgammaRIIb2 on a lymphoma cell

having a 1q21 abnormality., and the teachings of Latour et al on the endocytosis of antibodies via FcgammaRIIb2, and the teachings of Schlom et al which necessitate that the conjugated antibody be internalized in order for the drug, toxin or radionuclide to have a significant effect on the targeted tumor cell.

9. Applicant again argues that none of the cited references describes the IRTA2 protein of the instant claims. However, this arguments has been refuted for the reasons set forth above.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen A Canella whose telephone number is (571)272-0828. The examiner can normally be reached on 10 a.m. to 9 p.m. M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571)272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Karen A. Canella, Ph.D.
06/01/2004

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PRIMARY EXAMINER